REMARKS

I. PRELIMINARY REMARKS AND CLAIM AMENDMENTS

With this response, claims 1 and 43 have been amended to eliminate the requirement that the hydroxycitric acid be bound to calcium and potassium as the present invention is not so limited. Dependent claims 8 and 50 reciting those preferred compositions have been reintroduced as claims 105 and 106 and have been amended to reflect that the preferred composition comprises a dual salt of HCA with calcium and potassium. In addition, the dependencies of claims 32, 42, 74 and 84 have been modified and claims 33, 34, 58, 59, 72, 73, 75 and 76 have been canceled to simplify the issues before the Examiner.

II. THE OUTSTANDING REJECTIONS

Claims 1, 9-11, 18, 25, 32-34, 36-43, 51-53, 58-60, 66,67, 72-76, 78-85 and 93-106 are pending in the application. The rejections to the claims are set out below.

Claims 1, 9-11, 18, 25, 32-34, 36-43, 51-53, 58-60, 66,67, 72-76, 78-85 and 93-104 stand rejected under 35 USC 103(a) as being unpatentable over Raju, WO99/03464 in view of one or more of Policapellio, US 5,612,039; Allen, US 5,480,657; Alvia et al., US 6,413,545 and Briggs et al., US 2004/0204472.

Claims 1, 9-11, 18, 24 (sic 25?), 43, 51-53, 58-60, 66, 67, 72, 73, 85 and 93-97 stand rejected under 35 U.S.C. §102(e) as being anticipated by Bhaskaran et al., US 2003/0207942.

Claims 85-104 stand provisionally rejected for obviousness-type double patenting over InterHealth's USSN 09/463,024.

III. PATENTABILITY ARGUMENTS

A. The Rejection under 35 U.S.C. §112(second paragraph) Should be Withdrawn.

The rejection for indefiniteness under 35 U.S.C. §112 (second paragraph) should be withdrawn in light of the amendment of claims 8 and 50 to recite that the preferred composition comprises a dual salt of HCA with calcium and potassium.

B. The Rejection under 35 U.S.C. §103(a) Should be Withdrawn because there is no teaching in the art that administration of HCA would reduce ghrelin levels.

The rejection over Raju, WO99/03464 in view of one or more of Policapellio, US 5,612,039; Allen, US 5,480,657; Alvia et al., US 6,413,545 and Briggs et al., US 2004/0204472 should be withdrawn because the claims are directed to methods for decreasing ghrelin levels in subjects in need thereof by administering sufficient amounts of hydroxycitric acid (HCA) and there is no teaching in the art that administration of HCA would reduce ghrelin levels!

Each of Raju, Policapellio and Alviar teach that HCA promotes weight loss and Allen teaches that niacin-bound chromium promotes weight loss but none of these references teach that HCA (or chromium for that matter) decrease ghrelin levels.

Further, Briggs does not mention HCA much less teach that HCA decreases ghrelin levels. Instead, Briggs is cited as teaching that "antagonists of ghrelin receptors [are] effective as weight loss agents."

1. Briggs Teaches that Weight Loss Agents Can Have a Variety of Different Biological Activities Other than Ghrelin Receptor Antagonist Activity.

Briggs primarily teaches that COX-2 inhibitors are weight loss agents but does list ghrelin receptor antagonists among some 131 other weight loss agents for use in combination with COX-2 inhibitors.

Such weight loss agents include those with a wide variety of biological activities including (1) catecholamine modulators, (2) norepinephrine, dopamine and serotonin reuptake inhibitors, (3) lipase inhibitors, (4) dual serotonin reuptake inhibitors and serotonin releasing agents, (5) aminoketone class antidepressants, (6) activators of ATP-dependent K^+ channels, (7) anti-hyperglycemics, (8) GABA enhancer and sodium channel blockers, (9) serotonin and dopamine releasers, (10) histamine-3 antagonists, (11) cannabinoid (CB1) receptor antagonists, (12) alpha adrenergic receptor agonists, (13) melanocortin-4 receptor agonists, (14) neuropeptide Y antagonists, (14) beta(3)-adrenergic agonists, (15) glucagon-like peptide-1 agonists, (16) PPAR-gamma antagonists and PPAR-gamma partial antagonists, (17) urocortin agonists, (18) CCK agonists, (19) UCP activating

agents, (20) prolactin modulators, (21) growth-hormone secratagogues, (22) ciliary neurotropic factors, (23) antihistamines, (23) 5-HT_{2C} agonists, (24) 5-HT_{2A} agonists, (25) dopamine agonists, (26) adipocyte complement-related protein (Acrp30) modulators, (27) cannabinoid antagonists, (28) tyrosine phosphatase modulators, (29) 11beta hydroxysteroid dehydroxysteroid dehydrogenase type 1 modulators, (30) cyclic AMO response element-binding protein modulators, (31) diacylglycerol o-acyltransferase modulators, (32) fatty acid transport protein 4 modulators, (33) G protein beta-3 subunit 825T modulators, (34) high mobility group 1C modulators, (35) Kallikrein modulators, (36) melanin-concentrating hormone receptor modulators, (37) perilipin modulators, (38) Tub gene modulators, (39) anticonvulsants, (40) leptin receptor modulators, (41) metabolic accelerators, (42) adipogenesid modulating agents, (43) HK-a receptor antagonists, (44) PPAR-gamma antagonists, (45) PPAR-alpha agonists and (46) leptin agonists.

It is presumed that the Examiner is not arguing that all weight loss agents have all of the 46 activities listed above so that any given weight loss agent, such as HCA, would necessarily have ghrelin receptor antagonist activity. However, if that is not the Examiner's argument, then which activity (or activities) of the forty-six (46) listed would HCA be expected to have? Where is the teaching in the art that instructs one that HCA has ghrelin receptor antagonist activity instead of some other activity such as growth-hormone secratagogue activity or adipocyte complement-related protein (Acrp30) modulator activity or is an antihistamine or has any of a variety of other activities?

In the absence of some teaching (which has yet to be cited to) it becomes clear that the identification of ghrelin receptor antagonist activity is made only in hindsight based on Applicants' own disclosure. There is no evidence that a ghrelin receptor antagonist activity would have been predicted for HCA from an examination of the art prior to Applicants' invention. Accordingly, the rejection should be withdrawn.

2. Applicants Do Not Claim that HCA is a Ghrelin Receptor Antagonist!

What makes it particularly clear that hindsight is in play as the basis for the obviousness rejection is that Applicants' claims are not directed to "ghrelin receptor antagonist activity"! Instead, Applicants have demonstrated that administration of HCA reduces ghrelin levels! This is quite different from acting as a receptor antagonist. Indeed, one of ordinary skill in the art might just as readily predict that a presumed receptor antagonist would act to increase ghrelin levels (perhaps through a feedback effect) rather than decrease ghrelin levels. For this reason, the statement that "[d]ecreasing ghrelin levels is deemed to be an inherent property" is incorrect, not least of all because affecting a receptor (as a receptor antagonist) does not necessarily have any effect on the receptor's binding pair. Further, the citation to *Atlas Powder* is inapplicable because Applicants are not claiming a composition but rather a method.

For these reasons, the applied references would not teach one that administration of HCA would decrease ghrelin levels as recited and accordingly, the obviousness rejection based on the combination of Raju, Policapellio, Allen, Alvia and Briggs should be withdrawn.

C. The Rejection over Bhaskaran under 35 U.S.C. §102(e) Should be Withdrawn.

The anticipation rejection over Bhaskaran US 2003/0207942 should also be withdrawn because while Bhaskaran teaches administration of HCA to overweight subjects 1) most overweight subjects have low ghrelin levels (and would not appear to be in any need of reducing their ghrelin levels) and 2) many subjects with high ghrelin levels are not overweight.

1. Most (but not all) Overweight Subjects Have Low Ghrelin Levels and it is Unexpected that HCA Administration Would Lower Ghrelin Levels.

In general, overweight individuals are characterized by low ghrelin levels compared to normal weight individuals and underweight individuals, such as those suffering from anorexia nervosa, have high plasma ghrelin levels. Ghrelin, http://arbl.cvmbs.colostate.edu/hboods/pathphys/endocrin/gi/ghrelin.html (Attached hereto as Exhibit A) Thus, to the extent that Bhaskaran teaches administration of HCA to overweight subjects it would not be expected that HCA would lower ghrelin levels.

Moreover, not all (or even most) overweight subjects have high ghrelin levels and it is not clear that all overweight subjects need their ghrelin levels reduced. While many overweight subjects have low ghrelin levels (e.g., subjects suffering from nonalcoholic fatty liver disease tend to be overweight but have low ghrelin levels. *See* Marchesini et al., J. Clinical Endocrinology and Metabolism, vol. 88, No. 12, 5674-5679 (2003) (Attached hereto as Exhibit B)) others such as those suffering from Prader-Willi syndrome have plasma ghrelin levels that are "exceptionally high in comparison to patients similarly obese." (Exhibit A).

It is therefore unclear whether administration of HCA to the class of overweight subjects generally or overweight subjects suffering from nonalcoholic fatty liver disease will decrease ghrelin levels. In any event, there is no evidence that administration of HCA to overweight subjects in the prior art might not have invariably decreased ghrelin levels because the ghrelin levels might not be high and such invariability is necessary for inherent anticipation.[1] . Nevertheless, and in it absence, the rejection under 35 USC 102 must be withdrawn.

[1] Inherency may not be established by probabilities or possibilities. It is necessary for inherency that the missing subject matter " is necessarily present in the thing described in the reference ...it may not be established by probabilities or possibilities... The mere fact that a certain result may result from a given set of circumstances is not sufficient." MPEP 2163.07(a) *In re Robertson*, 49 USPQ 2d 1949, 1950-51 (Fed. Cir. 1999)

2. Many Subjects with High Ghrelin Levels are Not Overweight.

Similarly, many if not all subjects with high ghrelin levels are not overweight. Bhaskaran claims methods of reducing body weight by administering its HCA (claim 24) but it is widely known that those suffering from anorexia nervosa have high plasma levels of ghrelin. Misra et al., Am. J. Physiol Endocrinol Metab (March 8, 2005) attached hereto as Exhibit C. Additionally, ghrelin levels also tend to be high in patients who have cancer-induced cachexia. Wolf, et al., Cancer 106(4):966-73 (Feb 15, 2006) Abstract attached as Exhibit D.

Thus, any presumption based on Bhaskaran that a reduction in ghrelin levels will lead to weight loss or that weight loss is associated with a reduction in ghrelin levels is unsupported and contrary to the teachings of the art. Moreover, the discovery that HCA decreases ghrelin levels is of therapeutic interest beyond being a possible mechanism for weight loss in overweight individuals and could be of use in the treatment of non-overweight individuals suffering from high ghrelin levels, including possibly patients with cancer-induced cacheria or individuals suffering from anorexia nervosa.

For these reasons, the ability of HCA to reduce ghrelin levels is neither obvious in light of the prior art nor is it inherently anticipated by the teachings of that art and the rejections under 35 U.S.C. §102 and 103 should be withdrawn.

D. The Rejection for Obviousness-Type Double Patenting Should be Held in Abeyance.

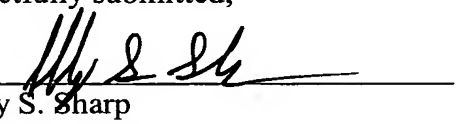
The provisional rejection of claims 85-104 for obviousness-type double patenting over copending US. Serial No. 09/463,024 should be held in abeyance pending the determination of patentability of one or the other application. Claims 1-2, 13, 15-16, 24, and 26-28 stand rejected under 35 U.S.C. §102(b) over the '692 patent.

IV. CONCLUSION

In view of the above amendment and remarks, applicants believe the pending application is in condition for allowance. Should the Examiner wish to discuss any issues of form or substance in order to expedite allowance of the pending application, she is invited to contact the undersigned at the number indicated below.

Dated: January 11, 2008

Respectfully submitted,



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